

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)
10 June 1998 (10.06.98)

International application No.
PCT/EP97/05897

Applicant's or agent's file reference
4 -21101/A

International filing date (day/month/year)
24 October 1997 (24.10.97)

Priority date (day/month/year)
28 October 1996 (28.10.96)

Applicant

TERSKIKH, Alexey et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

16 May 1998 (16.05.98)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

L. Panakal

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

REC'D 08 FEB 1999
WIPO PCT


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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4 -21101/A	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)	
International application No. PCT/EP97/05897	International filing date (day/month/year) 24/10/1997	Priority date (day/month/year) 28/10/1996
International Patent Classification (IPC) or national classification and IPC C12N15/62		
Applicant NOVARTIS AG et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 11 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application

Date of submission of the demand 16/05/1998	Date of completion of this report 04.02.99
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Meyer, W Telephone No. (+49-89) 2399-8157



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP97/05897

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-29 as originally filed

Claims, No.:

1-32 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 22 and 24.

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP97/05897

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☒ the claims, or said claims Nos. 22 and 24 are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-9 and 11-31.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP97/05897

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 7, 8, 12, 14-21, 23, 25 and 26
	No:	Claims 1-6, 9, 11, 13 and 27-31
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-9, 11-21, 23, 25-31
Industrial applicability (IA)	Yes:	Claims 1-9, 11-21, 23, 25-31
	No:	Claims

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. **Claims 22 and 24** are so inadequately supported by the description, that no meaningful opinion can be formed on the novelty, inventive step or industrial applicability of these claims (Article 34(4)(a)(ii) PCT. No indication in the description can be found, how a person skilled in the art should use the oligomers in order to induce apoptosis (**claim 22**), or to prevent tumour metastatization (**claim 24**).

Re Item IV

Lack of unity of invention

1. The international search report has been drawn up in respect of the entire international application, but the IPEA finds that the application does not comply with the requirement of unity of invention (Article 34(3) and Rules 13 and 68 PCT).
2. D1: Federation of European Biochemical Societies Letters, Vol. 341, pp. 54-58, 1994
D2: Journal of Molecular Biology, Vol. 211, pp. 943-958, 1990

Document D2 was not cited in the International Search Report.

3. An international application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.
Unity of inventions is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features, special technical features being such features, that define a contribution which each of the claimed inventions, considered **as a whole**, makes over the prior art.

4. The technical relationship among the independent **claims 1 and 10** is the application of an oligomerisation domain, which is not an antibody or a functional antibody fragment from the constant region. However, this relation cannot be accepted to consist of special technical feature as defined above since it does not define a contribution which each of the different claimed invention, considered as a whole makes over the prior art.
In fact, Document D1 discloses the use of the oligo-(i.e. penta-)merisation domain of Cartilage Oligomeric Matrix Protein for the pentamerisation of an additional methionine, or additional glutathiones. Both substances are low molecular weight substance and are not part of Cartilage Oligomeric Matrix protein (D1, Abstract).
5. Thus, the technical relationship of the independent claims does not embrace a special technical feature, within the meaning of Rule 13.2 PCT. The following inventions have to be considered separately:
 - (i) **Claims 1-9 and 11-32** refer to oligomers containing at least two units, each unit comprises a peptidic domain capable of oligomerising, wherein the oligomerising domain is not an antibody or a functional antibody fragment from the constant region and a domain capable of binding to an acceptor
 - (ii) **Claim 10** refers to the use of the pentamerisation domain of the Cartilage Oligomeric Matrix Protein for oligomerising of low molecular weight compounds or peptides.
6. The Applicant had been invited to restrict or to pay additional fees. The Applicant did not restrict nor pay additional fees. As the first invention indicated above appear to be of importance, the application will be prosecuted on the basis of the second mentioned invention, in other words the subject-matter of **claims 1-9 and 11-31**.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The examination relates to **claims 1-9 and 11-31** in so far as they involve an oligomer containing at least two units, each unit comprises a peptidic domain capable of oligomerising, wherein the oligomerising domain is not an antibody or a functional antibody fragment from the constant region and a domain capable of binding to an acceptor.
2. This preliminary opinion is being established under the assumption that the entire subject-matter is entitled to the claimed priority. If this is not the case, the 'P' document cited in the search report may have to be considered for novelty and/or inventive step. This document would appear to be detrimental to most, if not all, of the claimed matter (Article 33(2), (3) PCT).
3. The subject-matter of **claims 1-6, 9, 11, 13 and 27-31** is not new in the sense of Article 33(2) PCT.
 - 3.1 Independent **claim 1** has as subject-matter an oligomer comprising at least two units, wherein each individual unit comprises a peptidic domain and a domain capable of binding to an acceptor, wherein the oligomerizing domain is not an antibody or a functional antibody fragment from the constant region. The subject-matter is anticipated by Document D1, which discloses a protein, which forms an oligomer made of five units (D1, Abstract), wherein each unit comprises a peptidic domain capable of oligomerising and a domain capable of binding to an acceptor (D1, Abstract and Discussion), wherein the oligomerising domain is not an antibody or a functional antibody fragment from the constant region (D1, Abstract and Discussion).

- 3.2 The subject-matter of the dependent **claims 2-6, 9, 11, 13 and 27-31** are anticipated by D1, which discloses according to
- (i) present **claims 1 and 2**, an oligomer made of five units (D1, Abstract),
 - (ii) present **claim 5**, an oligomer, wherein each unit has 64 amino acids (D1, Abstract)
 - (iii) present **claims 4 and 6**, an oligomer, wherein a 43 amino acid long peptidic domain is capable of oligomerising. This domain ("acceptor") is capable of binding to an identical 43 amino acid long peptidic domain ("receptor"), both are connected via disulphide bridges ("spacer").
 - (iv) present **claims 9 and 13**, an oligomer, wherein "the individual units oligomerise spontaneously" under oxidizing conditions (D1, p. 56, right column, 1st paragraph)
 - (v) present **claim 11**, an oligomer, wherein the oligomerising domain is the pentamerisation domain of the Cartilage Oligomeric Matrix Protein (D1, Abstract)
 - (vi) present **claims 27-31**, a method for the synthesis or production of a peptide capable of pentamerisation, by the use of the microbiological host *E. coli*, comprising the expression vector p3b-COMP for the synthase of the peptide COMP. This synthesized peptide is able to pentamerise (D1, Material and methods)
4. The remaining dependent claims, in so far they can be understood (see VIII, below) which are directed to an oligomer, wherein at the C-terminus further a functional domain is attached (**claim 8**) or an oligomer, comprising units that bind to distinct acceptors (**claim 12**), appear to be concerned with mere technical variations of the not novel subject-matter of **claim 1**, and do not involve an inventive step in the sense of Article 33(3) PCT.
5. The subject-matter of **claim 7** does not involve an inventive step in the sense of Article 33(3) PCT. Document D1, which is considered to represent the most relevant state of the art, discloses a pentamer from which the subject-matter of **claim 7** differs in that a spacer is made of glutathione. The problem to be solved by the present invention may therefore be regarded as finding an alternative

spacer having a fixed structure. The subject-matter of the claim referred to above is considered to solve this problem.

However, the solution proposed in **claim 7** of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: D2 teaches the use of a spacer region, which is rich in the amino acid residue proline, providing an extended structure (D2, p. 947; p. 956, right column, second paragraph and Fig. 5). Thus a skilled person would try to use this spacer in order to solve the above mentioned problem. Consequently, **claim 7** does not fulfil the requirements of Article 33(3) PCT.

6. The subject-matter of **claims 14-20, 23, 25 and 26** cannot be considered as involving an inventive step in the sense of Article 33(3) PCT.

The claimed inventions refer to the use of a well-known product employing obvious properties of that product. It would be a matter of mere routine experimentation for a skilled person in the specific technical field to determine the claimed uses. Thus, the use of an oligomer for the identification (**claim 14**), for cell targeting (**claims 15 -17**), for inhibition of protein-protein interaction (**claim 18**), as a chelating agent (**claim 19**), as a cross linking agent (**claim 20**) for the construction of libraries (**claim 21**), intracellular inhibition of transcription factors (**claim 23**) and as a binding reagent in an enzyme immunoassay or radio immunoassay (**claims 25 and 26**) do not involve an inventive step in the sense of Article 33(3) PCT.

7. For the assessment of the present **claims 15-20, and 23** (and in their present wording also **claims 22 and 24**) on the question of whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of the claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new treatment.

Re Item VIII

Certain observations on the international application

1. The independent **claim 1** does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved (e.g. "An oligomercomprises a peptidic domain capable of oligomerizing") which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.
 - 1.1 Furthermore, **claim 1** lacks clarity (Article 6 PCT) in that the term(s)
 - "acceptor" is vague and not defined, since it is not clear what characterization or features such a substance should have. In a broad interpretation, it includes all chemical compounds which are able to interact with each other
 - "capable of oligomerizing"; are vague and not defined, since it is unclear which technical features are intended by the term "capable". In principle, any protein is capable of oligomerizing, by e.g. cross-linking.
 - "Peptidic domain" is not suitable to define clearly the scope of the claims. This term is without technical significance.
 - 1.2 It appears that the wording of **the dependent claims 2-9 and 11-31** does not remedy the clarity insufficiencies of the independent **claim 1**. Hence, those claims do not meet the requirements of Article 6 PCT.
2. The subject-matter of **claim 1** should be defined by means of positive features. A disclaimer may be used only when the claim's subject-matter cannot be defined more clearly and concisely by means of positive features (PCT Guidelines III 4.12).
3. **Claims 4 and 14** lack clarity due to the expression "acceptor or receptor". This wording is vague and not defined, since it is not clear what characterization or features such substances should have. Hence, this wording is open to individual interpretation (Article 6 PCT).

4. **Claim 7** lacks clarity due to the wording "proline-rich region". This wording is not suitable to clearly define the scope of the claim, because without a precise definition of the amount of prolines, this expression is vague and ambiguous (Article 6 PCT).
5. **Claim 9** does not meet the requirements of Article 6 PCT. The terms "oligomerize spontaneously" are vague, since it does not specify the conditions (temperature, salt, oxidizing, etc.) under which the oligomerisation occurs.
6. The denomination "Cartilage Oligomeric Matrix Protein" used in **claim 11** is arbitrary and thus is devoid of technical content. Consequently, when this term occurs in a claim, a reference to e.g. the corresponding SEQ ID NO or a reference to technical features should be provided (Article 6 PCT).
7. **Claim 12** lacks clarity due to the wording "distinct acceptor". This wording appears to be technically meaningless (Article 6 PCT).
8. The subject-matter of **claim 13** does not comprise any additional features when compared to that of **claim 1**. Therefore, **claim 13** appears to be superfluous.
9. **Claims 27 and 31** lack any true technical features which would properly define the claimed subject-matter. In the absence of clearly defined method step(s) such a claim cannot be accepted to be clear and comply with Article 6 PCT.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 4 -21101/A	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 97/05897	International filing date (day/month/year) 24/10/1997	(Earliest) Priority Date (day/month/year) 28/10/1996
Applicant NOVARTIS AG et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

- ☒ Certain claims were found unsearchable (see Box I).
- ☐ Unity of invention is lacking (see Box II).
- ☒ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 - ☒ filed with the international application.
 - ☐ furnished by the applicant separately from the international application,
 - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - ☐ Transcribed by this Authority

- With regard to the title,
 - ☐ the text is approved as submitted by the applicant.
 - ☒ the text has been established by this Authority to read as follows:

METHOD FOR THE OLIGOMERISATION OF PEPTIDES

- With regard to the abstract,
 - ☒ the text is approved as submitted by the applicant.
 - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

- The figure of the drawings to be published with the abstract is:
 - Figure No. ☐ as suggested by the applicant.
 - ☐ because the applicant failed to suggest a figure.
 - ☐ because this figure better characterizes the invention.
 - ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 97/05897

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Remark : Although claim 24 and claims 15-20, 22 and 23 insofar they concern an in vivo use, are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the oligomer.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/05897

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/62 C07K19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 26985 A (UNIV TEXAS) 12 October 1995 see page 9, line 5 - page 24 ---	1,4,5,9, 12-16, 18,23-31
X	WO 95 31540 A (MEDICAL RES COUNCIL ;H-J. HOPPE; K.B.M. REID) 23 November 1995 see page 19, line 9 - page 20, line 13 ---	1,4,5,9, 12-16, 23-31
A	A.V. KAJAVA: "Modeling of a five-stranded coiled coil structure for the assembly domain of the cartilage oligomeric matrix protein" PROTEINS, vol. 24, no. 2, February 1996, pages 218-226, XP000647810 see the whole document --- -/-	1-16

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

27 March 1998

Date of mailing of the international search report

07.04.98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Cupido, M

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	V.P. EFIMOV ET AL.: "The thrombospondin-like chains of cartilage oligomeric matrix protein are assembled by a five stranded alpha-helical bundle between residues 20 and 83" FEBS LETTERS, vol. 341, 1994, pages 54-58, XP002017642 see the whole document ---	1-16
P,X	WO 96 37621 A (MORPHOSYS GESELLSCHAFT FÜR PROTEINOPTIMIERUNG ; P. PACK ; A. HOESS) 28 November 1996 * paragraph bridging pages 18 and 19 * -----	1-18, 23-31

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 97/05897

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9526985 A	12-10-95	AU 2207195 A	23-10-95
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WO 9531540 A	23-11-95	AU 2451995 A	05-12-95
		CA 2190264 A	23-11-95
		EP 0757720 A	12-02-97
		JP 10500298 T	13-01-98
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WO 9637621 A	28-11-96	EP 0827544 A	11-03-98
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EP 97/05897


BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Ciba-Geigy AG
CH-4002 Basel

Institute of Biochemistry
University of Lausanne
155, Chemin de Boveresses
CH-1066 Epalinges

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR: SG13009/pSPXC6H	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 11236
II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION	
<p>The microorganism identified under I. above was accompanied by:</p> <p>(X) a scientific description (X) a proposed taxonomic designation</p> <p>(Mark with a cross where applicable).</p>	
III. RECEIPT AND ACCEPTANCE	
<p>This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on 1996-10-21 (Date of the original deposit)¹.</p>	
IV. RECEIPT OF REQUEST FOR CONVERSION	
<p>The microorganism identified under I above was received by this International Depositary Authority on (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).</p>	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):  Date: 1996-10-22

¹ Where Rule 6.4 (d) applies, such date is the date on which the status of international depositary authority was acquired.

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

EP 97/05897

INTERNATIONAL FORM

Ciba-Geigy AG
CH-4002 Basel

Institute of Biochemistry
University of Lausanne
155, Chemin de Boveresses
CH-1066 Epalinges

VIABILITY STATEMENT

issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Ciba-Geigy AG CH-4002 Basel Address: Institute of Biochemistry University of Lausanne 155, Chemin de Boveresses CH-1066 Epalinges		Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 11236 Date of the deposit or the transfer ¹ : 1996-10-21	
III. VIABILITY STATEMENT			
The viability of the microorganism identified under II above was tested on 1996-10-21 ² . On that date, the said microorganism was (X) ³ viable () ³ no longer viable			
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED⁴			
V. INTERNATIONAL DEPOSITARY AUTHORITY			
Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1b D-38124 Braunschweig		Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <i>U. Wehr</i> Date: 1996-10-22	

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

INTERNATIONAL SEARCH REPORT

Intern. Application No
PCT/EP 97/05897

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/62 C07K19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 26985 A (UNIV TEXAS) 12 October 1995 see page 9, line 5 - page 24 ---	1,4,5,9, 12-16, 18,23-31
X	WO 95 31540 A (MEDICAL RES COUNCIL ;H-J. HOPPE; K.B.M. REID) 23 November 1995 see page 19, line 9 - page 20, line 13 ---	1,4,5,9, 12-16, 23-31
A	A.V. KAJAVA: "Modeling of a five-stranded coiled coil structure for the assembly domain of the cartilage oligomeric matrix protein" PROTEINS, vol. 24, no. 2, February 1996, pages 218-226, XP000647810 see the whole document ---	1-16

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

27 March 1998

Date of mailing of the international search report

07.04.98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Cupido, M

INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/EP 97/05897

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	V.P. EFIMOV ET AL.: "The thrombospondin-like chains of cartilage oligomeric matrix protein are assembled by a five stranded alpha-helical bundle between residues 20 and 83" FEBS LETTERS, vol. 341, 1994, pages 54-58, XP002017642 see the whole document ---	1-16
P,X	WO 96 37621 A (MORPHOSYS GESELLSCHAFT FÜR PROTEINOPTIMIERUNG ; P. PACK ; A. HOESS) 28 November 1996 * paragraph bridging pages 18 and 19 * -----	1-18, 23-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 97/05897

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Remark : Although claim 24 and claims 15-20, 22 and 23 insofar they concern an in vivo use, are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the oligomer.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 97/05897

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9526985 A	12-10-95	AU 2207195 A	23-10-95
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WO 9531540 A	23-11-95	AU 2451995 A	05-12-95
		CA 2190264 A	23-11-95
		EP 0757720 A	12-02-97
		JP 10500298 T	13-01-98
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WO 9637621 A	28-11-96	EP 0827544 A	11-03-98
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